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USES OF STOCHASTIC MODELS IN THE EVALUATION OF POPULATION POLICIES. I. THEORY AND APPROACHES TO DATA ANALYSIS

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1. Introduction

During the past few decades, a number of workers have considered mathematical formulations for the reproductive performance of a group of women, or for some aspect of this performance (see [1] to [20] and reviews in [21], [22], [23]). These formulations have been intended to help in the appraisal of observed data, to yield estimators of some of the biological determinants of reproduction, or to predict effects of defined contraceptive practices, sterilization programs, and so forth. To date, explicit analytic results have been obtained only with considerable simplification of the underlying concepts, different workers resorting to different kinds of simplification. Alternatively, for greater realism, computer models are being developed, as discussed in the paper by E. B. Perrin in these *Proceedings* [56].

Sections 2 to 4 of this present paper will summarize work, done in collaboration with E. B. Perrin, on a class of mathematical models based on a relatively simple scheme for the process of human reproduction [9], [12] and will illustrate applications pertinent to efforts to reduce birth rates. Section 5 will illustrate issues arising in efforts to apply the results to empirical data, by using data from a simpler organism, the laboratory mouse, obtained in collaboration with D. P. Doolittle and M. New. Section 6 will present data on conception delays of a group of women, and an extension of a model previously presented for this phenomenon in a heterogeneous population [14].

Among the implications of such work, the greatest current interest probably lies in potential contributions to the evaluation of efforts to reduce birth rates—

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the predominant aim of "population policy" today. Such policy includes measures intended to influence birth rates either directly or indirectly, such as to: increase educational and employment opportunities for women, presenting attractive alternatives to large families; inform couples about contraceptive methods and supply the necessary means; provide easier access to induced abortion; or sterilize adults who meet defined criteria of age and parity. Though many considerations must enter into the evaluation of such policies [24], [25], we will be concerned only with methods that may contribute toward assessing the effectiveness of a specified program and toward predicting its effect on the birth rate.

2. Definition of the process

2.1. *General.* Since the social, economic, and psychological factors that affect birth rates can exert their effects only through modifying the biological determinants of the process [26], it is relevant to investigate the action of these biological determinants. The approach taken here attempts to do so. Also, it views the reproductive process as a sequence of events occurring to a cohort of women over a period of years. This viewpoint is different from and complementary to that underlying mathematical investigations of population growth such as stable population theory. Its rationale is straightforward: it seems to be a natural way of considering the action of biological factors, and even social factors; the advantages of regarding reproduction as a cohort phenomenon, in addition to examining annual cross sectional data, have been well established by experience [27]. Furthermore, since efforts to evaluate experimental "family planning" programs often consist of observations on a group of women followed from the inception of the program [28], [29], this viewpoint is especially relevant to methods used in evaluating such programs.

2.2. *Biological considerations.* In addition to the age when women begin their reproductive history and the duration of the reproductive span, the following biological factors call for consideration.

(1) *Fecundability* [1]. For a woman living in a sexual union, the probability that, during any ovulatory cycle, an ovum becomes fertilized and embedded (fecundability), depends on the interplay of many factors, including the use of contraceptives. Hence we may treat conception as a chance event, and the conception delay, or waiting time to conception [14], as a random variable. Despite a tradition that the norm for the length of the relevant biological time unit, the ovulatory cycle, is 28 days, there is evidence that its mean length is fairly close to a calendar month, 29.5 or 30 days [30], [31]. Hence we will equate the cycle to a calendar month, ignoring the appreciable variation between women and between cycles for any woman.

(2) *Outcomes of a pregnancy.* The importance of the variable incidence of pregnancy outcomes other than live births is obvious [16], [32]; in some situations, it is also desirable to distinguish between live births followed by death in

infancy and those followed by survival [33]. The probabilities of the various outcomes may vary with maternal age and health, rank order of the pregnancy, the time elapsed since the previous pregnancy, and the incidence of induced abortion.

(3) *"Lost time" or nonsusceptible periods.* A conception is followed by a period during which the woman is not susceptible to another conception. This "lost time" consists of pregnancy (gestation) plus the interval after its termination before resumption of ovulation [34], [35]. The outcome of a pregnancy is correlated with the durations of pregnancy and postpartum nonsusceptibility, while the latter depends also on breast feeding practices and their physiological impact [36], [37]. When ovulation is first resumed, it may be irregular, producing low fecundability. Subsequently, fecundability may increase gradually to assume its previous value or some new value.

On the basis of these considerations, the reproductive history of a woman may be taken to consist of passages through one or more mutually exclusive states (figure 1). At the beginning of a sexual union, she is nonpregnant and

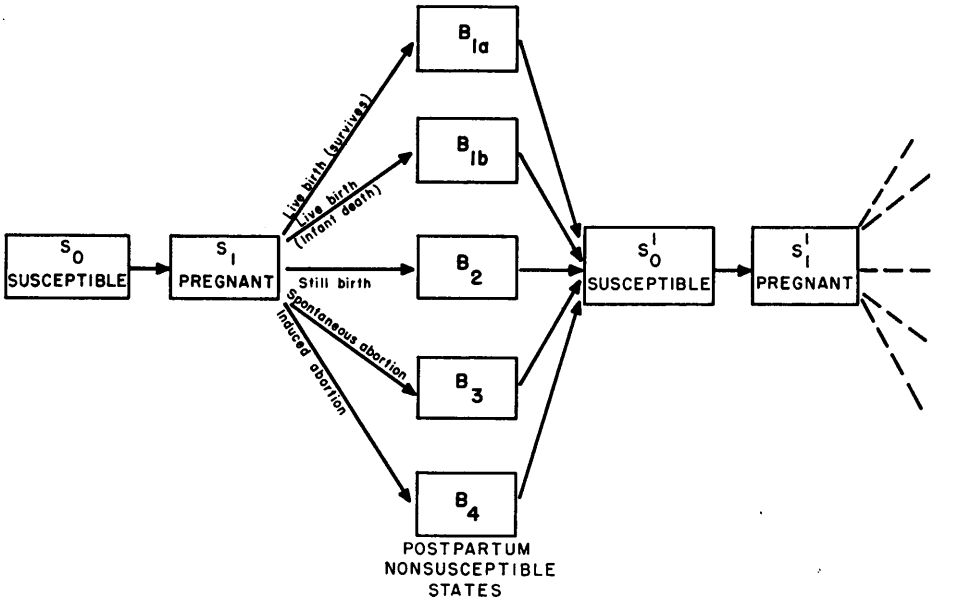

FIGURE 1

States in the reproductive history of a woman.

susceptible to conception (S_0). After a random period of time, she may enter pregnancy (S_1), from which she will enter the postpartum nonsusceptible state following a surviving live birth (B_{1a}), a live birth followed by early death (B_{1b}), a stillbirth (B_2) or an early fetal death (B_3 if spontaneous, B_4 if induced). After a stay of variable duration in any of these states, she again becomes susceptible,

passing to S_0' and so on, the primes indicating that each successive visit to a state may be different from earlier ones. The number of states B_i, that is, the number of possible outcomes of pregnancy considered, can depend on the detail needed for a specific purpose.

Clearly, a fecund woman must be in one and only one of these states at any time, and her reproductive history is characterized completely by the sequence in which the states are visited and by the length of time spent in each state at each visit. Accordingly, we seek models to describe the possible paths in this chain of events and the probability distribution of the number of transitions of each kind in time t.

3. A class of models

3.1. *Assumptions.* An approximation to this process, for which mathematical results are available, is shown in figure 2, where no distinction is made between the first and subsequent visits to any state (and where, for simplicity of presentation, the number of pregnancy outcomes included has been reduced). Models for processes involving "lost time" have been considered in the "counter problem" [38] and in other situations [39], [40].

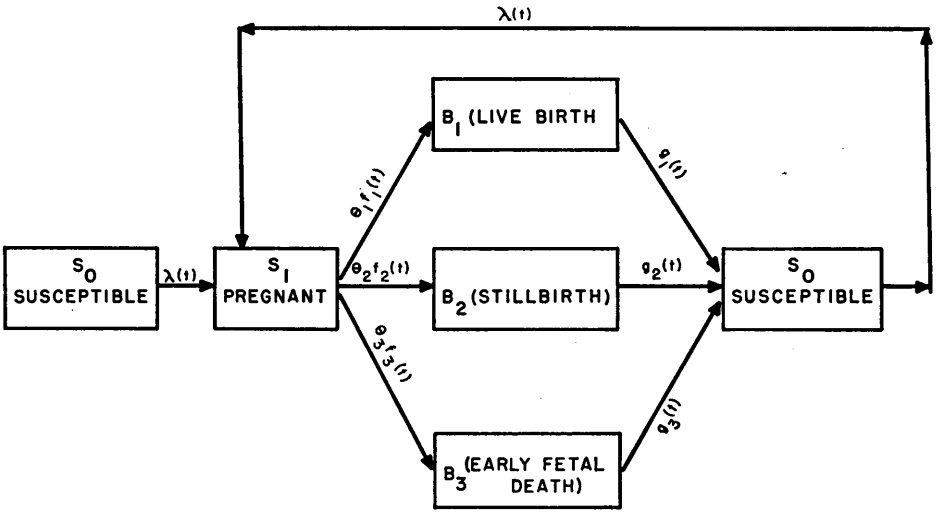

FIGURE 2

Probabilities of passage from one state to the next when length of stay at each state is considered as a random variable.

In figure 2, the length of stay in each state of the model is viewed as a random variable, the number of months spent in the susceptible nonpregnant state S_0 before passage to S_1 having the probability density $\lambda(t)$. The duration of stay in pregnancy (S_1) is assumed to depend on the outcome of the pregnancy, $f_i(t)$

being the (conditional) probability density of the number of months spent in S_1 given that the next state visited is B_i, and the density of the number of months spent in the postpartum state B_i being $g_i(t)$. Finally, θ_i is the probability that a given pregnancy ends with a transition to B_i.

The stationary process defined can be shown to be a semi-Markov or Markov renewal process (MRP) [40], [41], [42] with the specified states, the length of stay in any state being a random variable whose distribution function can depend on the state being occupied as well as on the next state to which the process will move. Further restrictions on the model provide special cases described elsewhere [9], [10], [12], [43]. As will be illustrated below, this formulation permits the moments of the passage times to be derived and hence yields the usual results for a renewal process, including asymptotic expressions for:

(1) the mean and variance of $N_i(t)$, the number of passages into a specified state (for example, the number of live births or of pregnancies) that occur in the interval $(0, t)$;

(2) the fertility rate or pregnancy rate per unit of time;

(3) the probability distribution of states after the process has continued for time t.

If it is assumed that the total "lost time" for each outcome has a fixed integral value, and that fecundability is constant, the foregoing may be reduced to a Markov chain, and explicit expressions derived for the probability distribution of the cumulative number of visits made to any state by time t.

3.2. *Results.* Since each passage time to any state can be expressed as a sum of a random number of random variables with all distributions specified, the mean and variance of the passage times may be derived by a straightforward probability argument [12]. Here, however, the methods of Pyke [41], [42], which give additional results, will be followed, with changes in notation.

Let

B_i be the postpartum nonsusceptible state that follows the ith type of pregnancy termination for $i = 1, 2, \cdots, a$;

θ_i be the probability that a given pregnancy ends in the outcome represented by B_i;

$\lambda(t)$ be the p.d.f. of the length of stay in S_0;

$f_i(t)$ and $g_i(t)$ the p.d.f., respectively, of the length of stay in S_1 and B_i given that passage from S_1 is to B_i;

L, F_i and G_i be the Laplace-Steiltjes (LS) transforms, respectively, of $\lambda(t)$, $f_i(t)$ and $g_i(t)$;

$\alpha_i^{(r)}$ be the rth moment of the compound distribution $\lambda(t)f_i(t)g_i(t)$;

W_i be $1 - L\sum_{j\neq i}\theta_j F_j G_j$;

M_{mn} the LS transform of the density function of the passage time from state m to state n;

$\mu_{mn}^{(r)}$ be the rth moment about zero of the passage time from state m to state n;

$N_j(t)$ be the number of visits made to state j in the interval $(0, t)$.

To derive the matrix M of the elements M_{mn} from which the moments of the passage times are obtained, as well as other results, we proceed as follows. Form the matrix Q as shown, with general postpartum states B_1 and B_j for $j = 2, 3, \cdots, a$, and elements Q_{mn} with $m, n = 1, 2, \cdots, a + 2$, consisting of LS transforms of the appropriate transition distributions as defined by Pyke and shown in [12]. For example, the probability that from pregnancy (S_1) the next passage will be to B_1 and will occur by time t is the transition distribution $\theta_1 \int_0^t f_1(x)\,dx$. Consequently,

$$Q_{23} = \theta_1 \int_0^\infty e^{-sx} f_1(x)\,dx = \theta_1 F_1. \tag{3.1}$$

TABLE I

MATRIX Q
(LS TRANSFORMS OF THE TRANSITION DISTRIBUTIONS)

From State	To State S_0	S_1	B_1	$\cdots$	B_j
S_0	0	L	0		0
S_1	0	0	$\theta_1 F_1$		$\theta_1 F_1$
B_1	G_1	0	0		0
.	.	.	.		.
.	.	.	.		.
.	.	.	.		.
B_j	G_j	0	0		0

The matrix M is given by

$$M = Q(I - Q)^{-1}\{\text{diag}\,[(I - Q)^{-1}]\}^{-1}, \tag{3.2}$$

where I is the identity matrix and diag $[A]$ is the matrix with diagonal elements A_{mm} and zeros elsewhere.

TABLE II

MATRIX M
(LS TRANSFORMS OF THE DENSITY FUNCTIONS OF THE PASSAGE TIMES)

From State	To State S_0	S_1	B_1	$\cdots$	B_j
S_0	$L\sum_i \theta_i F_i G_i$	L	$L\theta_1 F_1 / W_1$		$L\theta_j F_j / W_j$
S_1	$\sum_i \theta_i F_i G_i$	$L\sum_i \theta_i F_i G_i$	$\theta_1 F_1 / W_1$		$\theta_j F_j / W_j$
B_1	G_1	LG_1	$L\theta_1 F_1 G_1 / W_1$		$G_1 L\theta_j F_j / W_j$
.	.	.	.		.
.	.	.	.		.
.	.	.	.		.
B_j	G_j	LG_j	$G_j L\theta_1 F_1 / W_1$		$L\theta_j F_j G_j / W_j$

The moments of the passage times are obtained as

$$\mu_{mn}^{(r)} = (-1)^r M_{mn}^{(r)}(0), \tag{3.3}$$

where $M_{mn}^{(r)}(0)$ is the rth order derivative of M_{mn} with respect to s, evaluated at zero. In particular, the first two moments of the intervals between successive pregnancy outcomes B_i are

$$\mu_{ii}^{(1)} = \frac{1}{\theta_i} \sum_k \theta_k \alpha_k^{(1)} \tag{3.4}$$

and

$$\mu_{ii}^{(2)} = \frac{1}{\theta_i} \sum_k \theta_k \alpha_k^{(2)} + \frac{1}{\theta_i^2} \sum_k \theta_k \alpha_k^{(1)} \left[\sum_{j \neq i} \theta_j \alpha_j^{(1)} \right]. \tag{3.5}$$

If μ_{11} is the mean interval between live births, the asymptotic monthly fertility rate is given by [40]

$$\text{FR} \approx 1/\mu_{11}. \tag{3.6}$$

Among other results [12], these methods also yield the asymptotic probability P_{mn} of being in state n, given that the process began in state m. The matrix P is derived as

$$P = (I - Q)^{-1}(I - H), \tag{3.7}$$

where H is the diagonal matrix with $H_{mm} = \sum_n Q_{mn}$.

Rather than this matrix, however, we shall use results from a Markov chain formulation [38] of the process. Consider that a transition may occur at monthly intervals, between states:

S_0 nonpregnant, susceptible;

L_1 the month of conception leading to a live birth;

$L_2, L_3, \cdots, L_{m-1}$ the first, second, $\cdots$, $(m-2)$th month of nonsusceptibility leading to a live birth;

$A_1, A_2, \cdots, A_{w-1}$ the corresponding months relating to a conception leading to a fetal loss.

Let the transition matrix D be as shown, with $p + \pi + q = 1$ and $\lambda(t) = (1 - q)q^t$. The probability distribution of states occupied after the tth transition is given by the elements of D^t, the first row referring to the results when the process begins in S_0. For example, the probability of being in S_0 after the t transition is

$$\sum \sum \frac{(t - rm + r - vw + v)!}{r!v!(t - rm - vw)!} p^r \pi^v q^{t-rm-vw}, \tag{3.8}$$

where r and v assume all possible integral values that yield nonnegative exponents for the probabilities.

As $t \to \infty$ the probability distribution of being in the respective states at time t approaches

$$\begin{cases} \dfrac{1}{q + mp + w\pi}, & \text{for } S_0; \\ \dfrac{p}{q + mp + w\pi}, & \text{for } L_1, L_2, \cdots; \\ \dfrac{\pi}{q + mp + w\pi}, & \text{for } A_1, A_2, \cdots. \end{cases} \tag{3.9}$$

Accordingly, under this model approximately

$$[(m-1)p + (w-1)\pi](q + mp + w\pi)^{-1} \tag{3.10}$$

of the married, reproducing women will be nonsusceptible at any time after a reasonably long period since marriage, a portion of them becoming susceptible each month thereafter over a period of time. The results have implications both for the analysis of data on the distributions of births to a group of women in a calendar period [23] and for the planning and evaluation of family planning programs, as will be illustrated in section 4.

TABLE III

D TRANSITION MATRIX

	S_0	L_1	L_2	$\cdots$	L_{m-1}	A_1	A_2	$\cdots$	A_{w-1}
S_0	q	p	0		0	π	0		0
L_1	0	0	1		0	0	0		0
L_2	0	0	0		0	0	0		0
.	.	.	.		.	.	.		.
.	.	.	.		.	.	.		.
.	.	.	.		.	.	.		.
L_{m-1}	1	0	0		0	0	0		0
A_1	0	0	0		0	0	1		0
A_2	0	0	0		0	0	0		0
.	.	.	.		.	.	.		.
.	.	.	.		.	.	.		.
.	.	.	.		.	.	.		.
A_{w-1}	1	0	0		0	0	0		0

4. Applications of results

4.1. *Examples.* Probably the most fruitful applications so far of such results have consisted of operations with apparently realistic parameters (see [5] to [8], [10], [11], [13], [21], [32], [33], [43], [44]), to study the role of the various biological factors determining birth rates and to indicate approximate magnitudes of effects of changes in contraceptive use, abortion rates or the duration of the nonsusceptible periods. For example, it appears that unless a large proportion of a population adopts the use of contraceptives, highly effective methods are needed to lower the fertility rate appreciably (figure 3). Thus, on one set of assumptions, a contraceptive that reduces fecundability by 50 per cent

("effectiveness"), if used by even 70 per cent of all women, would reduce the asymptotic birth rate by less than 14 per cent. On the other hand, a contraceptive that is 70 per cent effective and is used by 50 per cent of the women would reduce the birth rate a little more, that is, by 18 per cent. Even a contraceptive with 95 per cent effectiveness would reduce the fertility rate by only 41 per cent if half the population used it and by only 82 per cent given universal use [10].

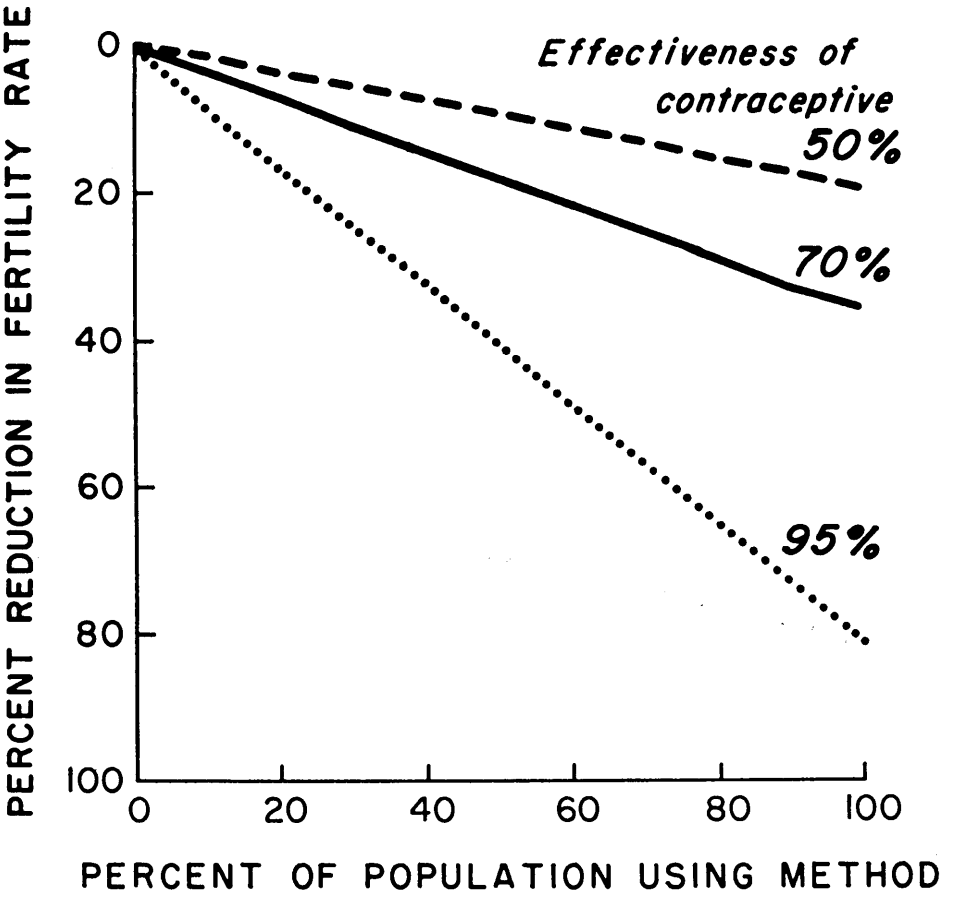

FIGURE 3

Reduction in fertility rate as a function of effectiveness of contraceptive and per cent of population using contraceptive.

The explanation of such findings is not too far to seek. With the postulated original parameters ($p = .18$, $\pi = .02$, $m = 18$ and $w = 5$), the "lost time" of 18 months, which is not subject to change by the adoption of contraceptives, constitutes more than 80 per cent of the original birth interval of 23 months.

A contraceptive that reduces fecundability by 70 per cent increases the mean interval between births only to 36 months; its effect on the asymptotic birth rate is correspondingly small. Thus, without contraception, the asymptotic number of conceptions expected per 1000 women per month is

$$1000(p + \pi)/(q + mp + w\pi) = 200/4.14 = 48.3 \tag{4.1}$$

and the corresponding number of live births is 43.5 (522 per year). With a contraceptive that reduces fecundability by 70 per cent the asymptotic monthly fertility rate will be 27.8/1000 acceptors, and, if 50 per cent of the women are acceptors, the asymptotic rate is 35.6 live births/1000 women in the population per month.

These are, however, long term effects. Consider what might happen at the beginning of a program. (This particular application was originally suggested by R. G. Potter.) Assume that a contraceptive program, initiated at time t_0, is accepted immediately by half the eligible women, and each woman permanently becomes an acceptor or nonacceptor. The contraceptive reduces fecundability by 70 per cent as above. Not all eligible women will be in the susceptible state S_0 at t_0, however. In fact, assuming that an equilibrium has been approached, we may estimate, from equation (3.9), that only about 24 per cent, on the average, of the women who would eventually be eligible for the program would be in S_0 at the time. During each of the next four months about 4.8 per cent of

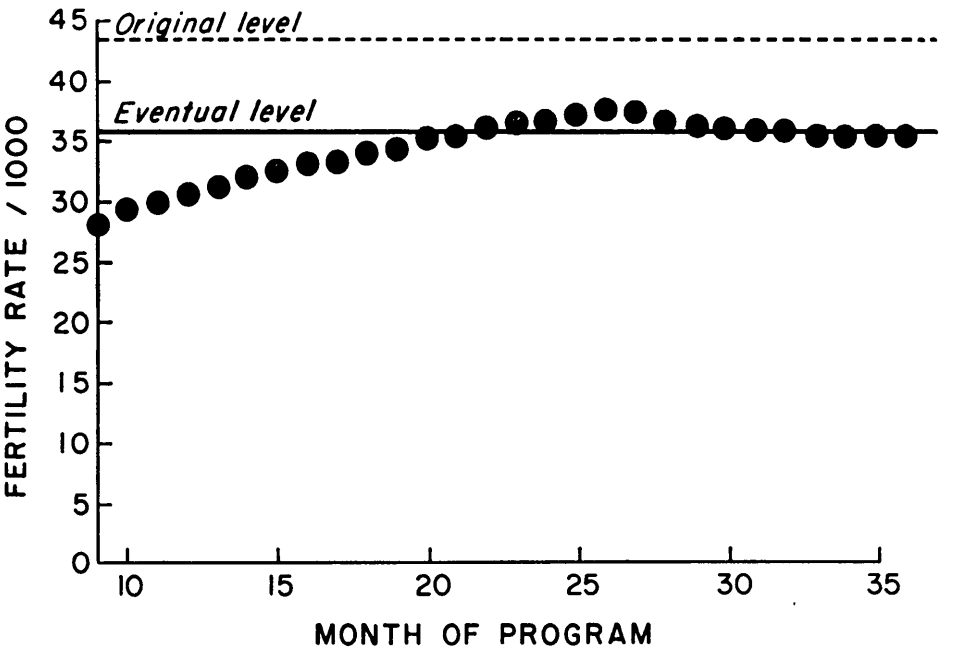

FIGURE 4

Expected increase in fertility as contraceptive program continues.

women would become newly eligible for the program and another 4.3 per cent for each of the 13 months after that. Assuming that 50 per cent of women become acceptors when they enter S_0, the rate of conception during the first month of the program and the live birth rate 9 months later would be about 20 per cent below the asymptotic levels to be reached eventually (figure 4). Thus, early results would give a deceptively optimistic impression, to be followed by a rise in these rates, disappointing if not expected.

Another illustration of how the models may be exploited is shown in table IV

TABLE IV

DISTRIBUTIONS OF NUMBER OF BIRTHS IN 10 OR 15 YEARS OF CONTRACEPTIVE USE

Fecundability = 0.01; postpartum nonsusceptibility six months.

	Fetal Mortality (per cent)	
	0	25
10 Year period		
Probability of		
0 births	.328	.437
At least 1 birth	.672	.563
At least 2 births	.253	.163
At least 3 births	.051	.024
At least 4 births	.005	.001
Mean number of live births	0.982	0.751
Variance	0.761	0.620
15 Year period		
Probability of		
0 births	.179	.280
At least 1 birth	.821	.720
At least 2 births	.466	.325
At least 3 births	.173	.091
At least 4 births	.041	.016
At least 5 births	.006	.001
Mean	1.508	1.214
Variance	1.161	0.949
Annual Fertility Rate/1000	105	81

(see also [43], [44]). Here it is assumed that, after achieving the size of family they desire, couples resort to a contraceptive that reduces fecundability to the constant monthly value of 0.01 and that the total lost time associated with a live birth lasts an average of 15 months. If there were no fetal deaths (the first column), the probability of avoiding any live births in a ten year period would be only 32.8 per cent, and the probability of at least two births 25.3 per cent. If such a contraceptive were used for fifteen years, the probability of at least one birth would be 82.1 per cent and the probability of at least three births, 17.3 per cent.

Results with a 25 per cent incidence of fetal death in such a population are shown in the next column. Even in this case, there would be less than a 44 per cent chance of avoiding any live births in a ten year period, and a 28 per cent chance of success in a fifteen year period. There is, in fact, almost a 10 per cent chance that, over a fifteen year period, three or more children would be born to a couple with a fetal loss rate of 25 per cent and a 1 per cent chance of conceiving in any month. With shorter nonsusceptible periods the results would be more discouraging. Again, it is clear that a high level of contraceptive effectiveness is necessary to ensure success in family planning.

Direct investigations of changes in fertility rates that would follow changes in incidence of fetal death are also of interest, both because improved health conditions may reduce this incidence and because induced abortion is a widely used means of limiting the size of families. Such investigations have indicated that the effects of a specified level of fetal loss are greater when fecundability is low than when it is high [11], [32]. Hence, a relatively high incidence of induced abortion may be expected to have an appreciably deflationary effect on birth rates only in populations that are also using contraceptive methods with some degree of effectiveness.

4.2. *Limitations.* Despite the considerable simplification involved, results such as the foregoing seem to be meaningful and useful. It is, however, natural to seek ways of making the models more realistic and applicable to empirical data on human reproduction. As given, they are not likely to be suitable for this purpose; in addition to the asymptotic character of many of the results, the models involve the untenable assumptions: that the women in a sample remain alive and fecund throughout the period of observation; that the intervals between births after the first have identical distributions regardless of age and parity; that the several parameters determining the distributions of the intervals are identical for all the women; and that changes in the parameters, as by contraceptive practices, are also uniform.

In what follows, two approaches will be explored to data for which such assumptions might *a priori* be considered fairly reasonable, and modifications in the assumptions considered.

5. An analysis of animal data

The number of litters born to 200 pairs of mice mated for 118 days under controlled conditions [45] is shown in table V. It was desired to examine the hypothesis that the observed variation in number of litters and in intervals between litters could arise in a group of mice with equal fecundity, against an alternative of varying fecundity, the term including all biological functions that affect the process. Given a renewal process for a homogeneous group of matings, asymptotic values for the mean and variance of the number of litters expected in t days are given by the expressions [46]

$$E[N_1(t)] \approx \frac{t}{\mu_{11}} + \frac{\mu_{11}^{(2)}}{2\mu_{11}^2} - \frac{\mu_{01}}{\mu_{11}} \tag{5.1}$$

and

$$\text{Var}\,[N_1(t)] \approx \frac{(\mu_{11}^{(2)} - \mu_{11}^2)t}{\mu_{11}^3} + \left[\frac{5(\mu_{11}^{(2)})^2}{4\mu_{11}^4} - \frac{2\mu_{11}^{(3)}}{3\mu_{11}^3} - \frac{\mu_{11}^{(2)}}{2\mu_{11}^2}\right] - \left[\frac{\mu_{11}^{(2)}\mu_{01}}{\mu_{11}^3} - \frac{\mu_{01}^{(2)} - \mu_{01}^2}{\mu_{11}^2} - \frac{\mu_{01}}{\mu_{11}}\right], \tag{5.2}$$

where $\mu_{01}^{(r)}$ and $\mu_{11}^{(r)}$ represent the rth moment about zero of the first and subsequent intervals respectively, and the means do not carry superscripts. Values

TABLE V

DISTRIBUTION OF 200 PAIRS OF MICE, BY NUMBER OF LITTERS BORN IN 118 DAYS

Number of Litters n	Number of Matings with n Litters
0	2
1	5
2	0
3	12
4	28
5	143
6	10
Mean Number of Litters/Mating = 4.6;	Variance = 0.96

for (5.1) and (5.2) were calculated with the moments of the observed intervals to the first litter and between litters 1 and 2 and 2 and 3, namely,

$$\begin{aligned} \mu_{11} &= 21.4 \text{ days}, & \mu_{01} &= 22.9 \text{ days}, \\ \mu_{11}^{(2)} &= 480.0, & \mu_{01}^{(2)} &= 592.0. \\ \mu_{11}^{(3)} &= 11610, \end{aligned} \tag{5.3}$$

For $t = 118$, the results were estimated $EN(t) = 5.0$ and estimated Var $N(t) = 0.44$, the latter value being less than half of the observed variance (table V).

It is known [12], however, that the exact values of the mean and variance for finite t tend to fluctuate around (5.1) and (5.2). Consequently, the mean and variance of the cumulative number of litters per mating observed on each day of the experiment were calculated, as shown in figure 5 together with the regression lines (5.1) and (5.2).

The relatively good agreement of observed results and "expected" values in the earlier part of the experiment of course follows from the calculations; the "test" is the fit in the latter part of the experiment. As time goes on, the observed means seem to be a little low. The observed variance is appreciably in excess of the theoretical asymptotic results. Although results for a longer period

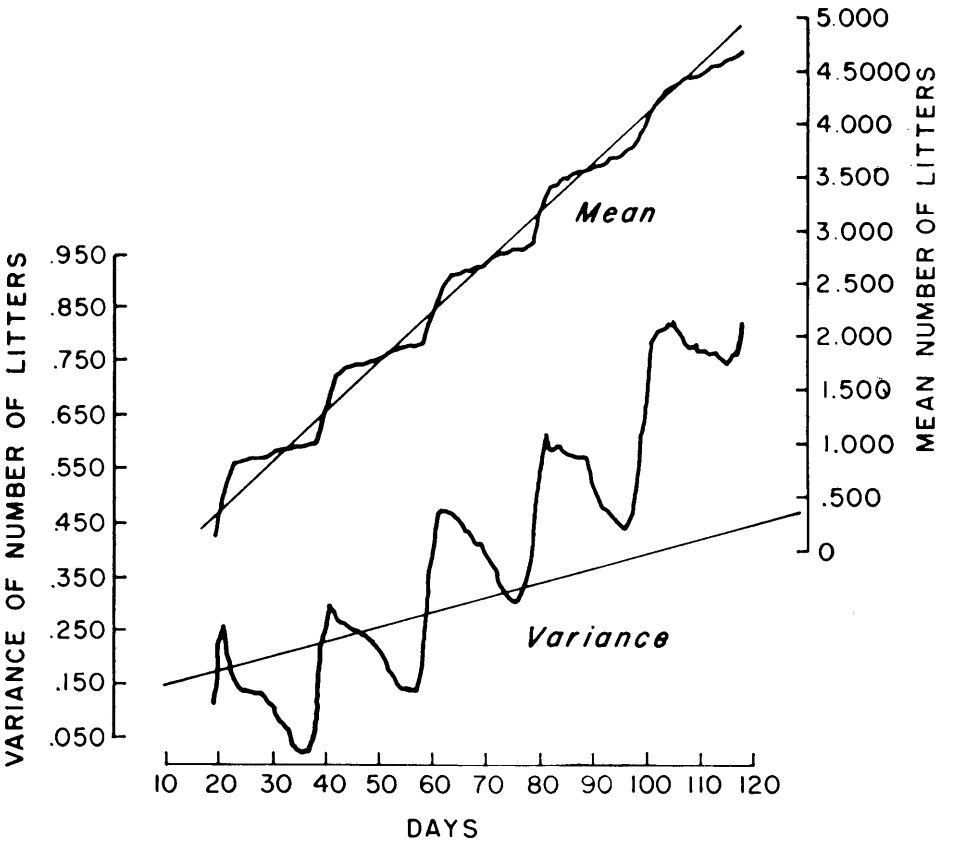

FIGURE 5

Mean and variance of the cumulative number of litters per mating compared with their estimated values from (5.1) and (5.2).

would be desirable, the data suggest that the hypothesis of a homogeneous, stationary process should be rejected. It should, however, be noted that the appropriateness of the values (5.3) may be questioned, since they are based on only 198 first intervals and 193 second intervals. A possible alternative is analysis of the subgroup of matings formed by discarding the seven who had fewer than three litters, using the distributions of their intervals. This analysis does yield a better fit, as reported elsewhere [47]. The exact distribution of $N(t)$ for $t = 1, 2, \cdots, 118$, on similar assumptions is also being investigated.

In general, this preliminary analysis would seem to indicate that:

(a) though it may be possible to derive an impression about the suitability of these models for a specific set of data, improved methods of examining such a hypothesis are needed;

(b) in this group of 200 pairs of mice, which come from a random mating

stock derived from the cross of four inbred lines, the evidence raises doubts about the existence of a homogeneous stationary process.

6. Conception delays in a heterogeneous human population

6.1. *The data.* The skepticism already expressed about the suitability of the assumptions in homogeneous stationary models for human reproductive data suggests a first approach to only part of the process. Consequently, we will here confine ourselves to data on conception delays [14]. Such data are important in their own right, since they provide a means for studying fecundability, whether natural or as affected by contraceptives [29].

It is customary, with some substantive justification, to assume, as was done in section 4, that, within a homogeneous population, the conception delay (X) is distributed geometrically, that is, $\lambda(x) = \rho(1 - \rho)^x$. Available evidence, however, raises doubts about the assumption of homogeneity, not only for women using contraceptives, but even for apparently noncontracepting women. For example, the data in table VI refer to 342 women in such a population [37],

TABLE VI

DISTRIBUTION OF ESTIMATED CONCEPTION DELAYS IN 342 WOMEN

Delay in Months	Number of Women Still Eligible	Number Conceiving	Proportion of Eligible Women Conceiving
0	342	103	.301
1	239	53	.222
2	186	43	.231
3	143	27	.189
4	116	30	.259
5	86	9	.105
6	77	12	.156
7	65	9	.138
8	56	6	.107
9	50	8	.160
10	42	10	.238
11	32	5	.156
12	27	2	.074
13	25	6	.240
14	19	1	.053
15	18	1	.056
16–53	17	17	—
Mean Delay 3.75 Months;		Variance = 30.47	

who had a live birth at least nine months after marriage and who denied having an intervening pregnancy. In an attempt to select a homogeneous group, women aged above 25 years at marriage were excluded. The conception delay was estimated by subtracting nine months from the interval between marriage and the first live birth. The last column in table VI shows the estimated proportion

of women conceiving in each successive month, out of those still at risk. (I am indebted to Dr. Arthur G. Steinberg of Western Reserve University for these human data.)

Data on conception delays usually show a marked tendency for the monthly incidence of conception among eligible women to decrease with time [13], [16]. Table VI does not do so unequivocally, but a suggestion of such a trend is present. Since a simple geometric distribution observed for t months is equivalent to a two state Markov chain undergoing t transitions, the hypothesis H_0: $\lambda(x) = \rho(1 - \rho)^x$ is equivalent to H_0: $p_{ij}(x) = p_{ij}$ for $i, j = 1, 2$. It has been shown that, under H_0, if the data in a Markov chain with s states are arranged to resemble an s by t contingency table, the numbers in state i at time x being treated like numbers in independent samples, the statistic calculated as a contingency chi square is distributed asymptotically as χ^2 with $(s - 1)(t - 1)$ degrees of freedom (d.f.) [48]. Further, this statistic can be broken down into single independent values distributed as χ^2 with one d.f. [49]. Using this test, H_0 is rejected, at the $P < .05$ level on the data for months 0 and 1 in table VI.

Furthermore, since in a homogeneous geometric distribution, with a mean waiting time (conception delay) $\bar{x}$, the variance is expected to equal $\bar{x}(\bar{x} + 1)$ [14], [38], the variance in this case would be expected to be approximately $(3.75)(4.75) = 17.81$, a value considerably below the observed variance of 30.47.

Such findings may be due in part to the method of estimation, or to reporting errors with respect to dates or intervening pregnancy wastage. More important, fecundability may vary from one month to the next in one woman, even in a relatively short period, and is likely to vary between women. We shall now examine the consequences of this last possibility.

6.2. *A model for conception delays in a heterogeneous group.* Assume that the monthly probability of conceiving ρ is constant for each woman during the period of observation, but varies between women, being distributed as $\varphi(\rho)\, d\rho$, and the conception delay X being a random variable given by the compound geometric distribution [50]

$$\lambda(x) = \int_0^1 \rho q^x \varphi(\rho)\, d\rho, \tag{6.1}$$

where $q = 1 - \rho$. It has been shown [14], that in such a distribution, the expected "hazard rate," or monthly probability of conception for the sample as a whole is a decreasing function of time, and maximum likelihood estimators of the moments of q have been derived from the numbers conceiving in successive months. In general, compound distributions have been studied by the method of moments [51] which has been applied to compound negative binomial distributions in [50], [52], and [53]. The moments estimated in these works are, however, moments not of q or ρ but of variables that correspond to q/ρ, though the notation varies. Published results include expressions corresponding to (6.3) and (6.4) below and a discussion has been given [54] of the characteristics of the estimators in an analogous compound exponential distribution.

Let
ρ be the fecundability, distributed as $\varphi(\rho)\,d\rho$;
$q = 1 - \rho$;
$\gamma = q/\rho$;
EY^r be the expected value of the r.v. Y^r and VY its variance;
$m_{[r]}$ be the rth factorial moment of a variable;
$K_{[r]}$ the corresponding cumulant;
X the conception delay;
s_x^2 the variance of the conception delays in a sample of size n, that is, $s_x^2 = \sum_{j=1}^{n} (x_j - \bar{x})^2/(n-1)$;
c be the mean value of γ in a sample, that is, $c = \sum_{j=1}^{n} (1 - \rho_j)/\rho_j n$;
$c^{(2)}$ be the variance of γ in a sample, defined as $[\sum \gamma_j^2 - (E\gamma_j)^2/n]/n$.

From (6.1), the probability generating function (p.g.f.) of X is

$$\sum_{x=0}^{\infty} \lambda(x)s^x = \int_0^1 \rho(1 - qs)^{-1}\varphi(\rho)\,d\rho. \tag{6.2}$$

Successive differentiation of (6.2) with respect to s, and evaluation at $s = 1$, gives the generalized factorial moment of X, in agreement with [50] and [53], as

$$m_{[r]} = EX(X-1)\cdots(X-r+1) = r!E\gamma^r \tag{6.3}$$

and consequently, as in [14],

$$\begin{aligned} EX &= E\gamma, \\ EX^2 &= 2E\gamma^2 + E\gamma, \\ VX &= 2V\gamma + E\gamma(E\gamma + 1). \end{aligned} \tag{6.4}$$

Assume that in a random sample of n women, the jth woman has parameter ρ_j and the corresponding parameter $\gamma_j = q_j/\rho_j$. The observations from such a sample are conception delays X_j. The moments of each X_j are as in (6.4) with $E\gamma_j^r = \gamma_j^r$. Since the conception delays X_j are mutually independent, the p.g.f. for the sum of X_j in the sample is

$$\Psi(s) = \prod_{j=1}^{n} \rho_j(1 - q_j s)^{-1}. \tag{6.5}$$

The factorial cumulants of the sum, obtained by successive differentiation with respect to s of $\log \Psi(s)$ and evaluation at $s = 1$ [55], are given by

$$K_{[r]}(\sum X_j) = (r-1)! \sum_{j=1}^{n} \gamma_j^r. \tag{6.6}$$

Hence, for a given sample,

$$E[(\sum X)^2] = \sum \gamma_j^2 + \sum \gamma_j + (\sum \gamma_j)^2 = n[c^{(2)} + c + (n+1)c^2]. \tag{6.7}$$

Conditional on the sample, from (6.4) and (6.7), the variance of the conception delays is

$$(6.8)\qquad E(s_x^2|\text{sample}) = \frac{1}{n-1}\left[\sum_{j=1}^{n}(2\gamma_j^2+\gamma_j) - \frac{1}{n}\sum_{j=1}^{n}(\gamma_j^2+\gamma_j) - \frac{1}{n}\left(\sum_{j=1}^{n}\gamma_j\right)^2\right]$$
$$= \frac{2n-1}{n(n-1)}\left[\sum\gamma_j^2 - \frac{(\sum\gamma_j)^2}{n}\right] + c^2 + c.$$

The unconditional expectation, since $Ec^{(2)} = (n-1)V\gamma/n$ and $Ec^2 = (E\gamma)^2 + V\gamma/n$, is

$$(6.9)\qquad E(s_x^2) = 2E\gamma^2 + E\gamma - (E\gamma)^2 = 2V\gamma + E\gamma(E\gamma+1).$$

Accordingly, (6.10) and (6.11) provide estimators of the variance of γ within a sample and in the universe, as

$$(6.10)\qquad \hat{c}^{(2)} = \frac{n-1}{2n-1}[s_x^2 - \bar{x}(\bar{x}+1)],$$
$$\hat{V}\gamma = \frac{1}{2}[s_x^2 - \bar{x}(\bar{x}+1)],$$

as in [14]. The estimators (6.10) are biased, an unbiased estimator being

$$(6.11)\qquad V^*\gamma = \frac{1}{2}\left[\frac{n+1}{n}s_x^2 - \bar{x}^2 - \bar{x}\right].$$

In a homogeneous population, under the assumption of a simple geometric distribution, the expected value of (6.11) is, of course, equal to zero.

6.3. *Applications to the data.* From (6.4) and (6.11) $\hat{E}\gamma\pm$ its standard error is 3.75 ± 0.27 and $V^*\gamma = 6.37$. The harmonic mean ρ is estimated as $1/(3.75 + 1.00) = 0.211$. The estimator of the arithmetic mean of ρ is equal to the proportion of women conceiving in the first month, that is, to 0.301, while the variance of ρ may be estimated [14] from the proportions conceiving in the first two months as

$$(6.12)\qquad \hat{V}\rho = .301(1-.301) - \frac{53}{342} = 0.055.$$

Thus, it appears that, even for this group of women in the relatively short period of observation, the data depart from a simple geometric distribution of conception delays. Not only are both the mean conception delay and its variance considerably in excess of what would be expected from the proportion conceiving in the first month, but the variance appreciably exceeds that expected in a simple geometric distribution with a mean conception delay of 3.75 months. Hence, we may expect the reproductive performance of this sample to have a lower mean and greater variation than would be predicted from a geometric distribution with parameter 0.211.

More general inferences about the effects of heterogeneity on birth rates are suggested by the fact, as indicated in equation (5.1), that the expected parity of a homogeneous group in time t is a function of the reciprocal of the mean interval between successive births. Suppose that in a heterogeneous population

with varying mean intervals between successive births, the arithmetic mean interval is $\bar{\mu}$ and the harmonic mean μ'. Then the average parity might be expected to be a function of $1/\mu'$, which is greater than $1/\bar{\mu}$. Further investigations into the effect of heterogeneity on birth rates are clearly indicated.

7. Summary and conclusions

A class of mathematical models for reproduction has been formulated for a homogeneous cohort of women on the assumption that the process is independent of age and parity. A summary is presented of these models, as developed in collaboration with E. B. Perrin. Despite simplification in the models, the results provide a useful means of investigating the approximate magnitude of the changes in birth rates that may be expected to follow various patterns of contraceptive practice or changes in abortion rates. Hence, they may be useful both in the formulation of population policy and in efforts to evaluate the effects of a specified program. Illustrations of such applications are given.

The assumptions in these models are, however, believed to be too restrictive for direct application of the results to human data. An attempt is presented to fit a similar model to reproductive data from a simpler organism, the laboratory mouse (from experiments performed in collaboration with D. P. Doolittle and M. New). While the test is not definitive, the results suggest that the reproductive performance of this sample of a random mating stock of mice derived from a cross of four inbred lines does not conform to a stationary homogeneous process.

Another set of data presented consist of the estimated conception delays to first conception in 342 noncontracepting women (data obtained through the courtesy of A. G. Steinberg). It seems clear that an assumption that all these women have the same constant monthly probability of conception is untenable. A model is presented for the distribution of conception delays in a group where this probability remains constant for any women but varies between women in an unspecified manner, and the moments of the underlying distribution are estimated.

In summary, models for which explicit analytic solutions are at present available have led to valuable insights into many questions relevant to the formulation and evaluation of population policy. There is a need, however, for more realistic, less restricted models. One avenue of investigation into such more general formulations lies in pursuing and extending the implications of less restrictive assumptions by mathematical analysis. Another method of studying these more general situations lies in the exploitation of computer models.

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